

## REMARKS/ARGUMENTS

### I. Introduction

Applicants acknowledge receipt of the Non-Final Office Action mailed February 10, 2005. Applicants thank the Examiner for withdrawing most of the Examiner's previous objections and rejections in light of Applicants' response filed October 25, 2004. Claims 36-48 and 51-87 are currently pending in the application. Claims 1-35 were canceled in the Preliminary Amendment filed August 3, 2001. Claims 77-85 were allowed in the Non-Final Office Action of July 1, 2004. Claims 49 and 50 have been canceled. Claims 36-38, 51-55, 77-79, and 81-87 stand rejected. The Examiner has objected to claims 39-48, 56-76, and 80.

### II. The Examiner's Rejections

#### A. Rejections Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

The Examiner has rejected claims 36-38 and 51-55 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-31 and 48-49 of U.S. Patent No. 6,821,726. Applicants submit herewith a terminal disclaimer overcoming such rejection. Therefore, the rejection of claims 36-38 and 51-55 should be rendered moot.

#### B. Rejections Under 35 USC § 102(b)

The Examiner has rejected claims 77-79 and 81-86 under 35 USC § 102(b) as being anticipated by Ayres *et al.* (U.S. Patent No. 3,945,928). The Examiner has alleged that Ayres *et al.* disclose a tubular container closed at both ends and divided into two chambers, with a flexible flap valve edge fixed to the barrier between the two chambers and the other portion of the edge free, wherein the flap, when subjected to a centrifugal force, flexes away from the valve seat, and upon cessation of the centrifugal force, returns to its normal position to seal the passageway

between the two chambers (claim 1). The Examiner has further alleged that regarding claims 81 and 82, it is reasonable to conclude that the thickness of the flap would fall between 1-5 mm, given the scale of the drawing provided.

Applicants respectfully traverse this rejection. Applicants remind the Examiner that claims 77-85 were previously allowed in the Non-Final Office Action of July 1, 2004. Claims noted as allowable shall thereafter be rejected only after the proposed rejection has been submitted to the primary examiner for consideration of all the facts and approval of the proposed action. Great care should be exercised in authorizing such a rejection. *See Ex parte Grier*, 1923 C.D. 27, 309 O.G. 223 (Comm'r Pat. 1923); *Ex parte Hay*, 1909, C.D. 18, 139 O.G. 197 (Comm'r Pat. 1909). MPEP § 706.04. Applicants respectfully submit that although the Examiner has cited Ayres *et al.* for allegedly anticipating claims 77-79 and 81-86 of the present invention under 35 USC § 102(b), the Examiner has not provided the proper paragraph for rejecting the previously allowed claims over new prior art (i.e., ¶ 7.50 of MPEP § 706.04).

Furthermore, Applicants submit that Ayres *et al.* do not meet all of the limitations of claims 77-86. In order to reject a claim under 35 USC § 102, the Examiner must demonstrate that each and every claim element is contained in a single prior art reference. *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986); *see also* MPEP § 2131 (August 2001). Claim terms are to be given their plain meaning as understood by the person of ordinary skill in the art, particularly given the limitations of the English language. *See* MPEP §§ 707.07(g); 2111.01 (August 2001). Not only must the claim terms, as reasonably interpreted, be present, an allegedly anticipatory reference must enable the person of ordinary skill to practice

the invention as claimed. Otherwise, the invention cannot be said to have been already within the public's possession, which is required for anticipation. *See Akzo, N.V. v. U.S.I.T.C.*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); *In re Brown*, 141 USPQ 245, 249 (CCPA 1964).

Ayres *et al.* disclose a centrifugation vessel divided by a centrifugal valve (col. 1, lines 51-54; col. 2, lines 52-55; col. 4, lines 29-31). Ayres *et al.* disclose a flap, but the flap does not divide the upper and lower chambers of the tube. Rather, the flap is merely attached by one edge to the centrifugal valve barrier of the tube. In contrast, claim 77 of the instant invention teaches a centrifugation vessel divided by a flap. Applicants submit that in light of this distinguishable feature of claim 77 over Ayres *et al.*, claim 77 should be allowable, and therefore, claims 78-86, which depend from claim 77, should also be allowable because they further limit claim 77.

**C. Rejections Under 35 USC § 102(e)**

The Examiner has maintained the rejection of claim 87 under 35 USC § 102(e) as being unpatentable over Ts'o *et al.* for the same reasons mentioned in the Non-Final Office Action of July 1, 2004. In the Non-Final Office Action of July 1, 2004, the Examiner alleged that Ts'o *et al.* teach the isolation and *in vitro* culturing of rare (cancerous) cells and allegedly disclose a method for the enrichment of cancer cells from a body fluid, comprising centrifuging the body fluid in a cell separation medium to separate the tumor cells from the blood.

The Examiner has also maintained that Ts'o *et al.* allegedly disclose examples of body fluids such as blood, urine, saliva, lymph, spinal fluid, semen, amniotic fluid, cavity fluids, and tissue extract, and that the rare cells are cancer cells from localized and non-localized cancer, including carcinomas of the brain, breast, bladder, colon, kidney, liver, lung, ovary, pancreas, prostate, rectum, and stomach, in addition to sarcomas, cancerous hematopoietic cells,

melanomas, teratocarcinomas, neuroblastomas, and gliomas. The Examiner has further alleged in the Non-Final Office Action of February 10, 2005 that because T'so *et al.* disclose the culture of tumor cell lines obtained by the claimed methods, and because claim 87 is a product-by process-claim, the tumor cells isolated by the method of T'so *et al.* would have the same characteristics as the corresponding tumor cells isolated by the method of claim 36.

Applicants respectfully traverse this rejection. The patentability of a product does not depend on its method of production. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Rather, patentability of product-by-process claims is based upon the patentability of the product itself, not the process. See MPEP § 2113 (Rev. 1, Feb. 2003).

Applicants respectfully submit that the patentability of the tumor cell culture of claim 87 should not be based upon the process of claim 36. Although T'so *et al.* teach that rare cells can be cultured, the Examiner has not shown why the culture allegedly disclosed in T'so *et al.* anticipates the tumor cell culture of claim 87, obtained by the method of claim 36, or that the tumor cells isolated by the method of T'so *et al.* have the same characteristics as the corresponding tumor cells isolated by the claimed methods.

Even if the Examiner maintains that the patentability of claim 87 should depend upon the process of claim 36, and is of the opinion that the process of claim 36 is anticipated by the process taught by Ts'o *et al.*, Applicants argue that Ts'o *et al.* do not anticipate claim 36 because Ts'o *et al.* do not teach every element of claim 36. Applicants maintain that claim 36 recites a single-step enrichment procedure for tumor cells that provides an important advantage over the teaching of Ts'o *et al.* because this single-step procedure makes it possible to enrich disseminated tumor cells of different types of tumor-like carcinoma cells from the colon, non-small cell lung

cancer, mammacarcinoma, and prostate carcinoma cells. At the same time, this procedure significantly reduces unwanted blood cells which might interfere with further diagnostic steps and negates the need for further purification steps, such as those taught in Ts'o *et al.*

In contrast, Ts'o *et al.* teach a comparatively complicated two-step enrichment procedure, comprising a method of enriching cancer cells (i.e., prostate cancer cells) in a body fluid sample using a multiple-step density gradient centrifugation process, wherein the density gradient separations are carried out at least twice (col. 6, lines 19-25; col. 10, lines 1-4). This centrifugation process may result in four to six different regions including a plasma, interface, gradient, and cell pellet which comprises a first fluid. The gradient and interface are then subsequently combined to produce more collection fluids. Ts'o *et al.* also do not teach the simultaneous enriching of tumor cells and depleting of unwanted blood cells from a body fluid or a centrifugation vessel that is separated by a porous barrier, a filter, a sieve, or a flap into an upper compartment and a lower compartment, wherein the body fluid is in the upper compartment and the cell separation medium is in the lower compartment, as in claim 36.

Thus, Applicants submit that because Ts'o *et al.* do not teach all of the limitations of claim 87, Ts'o *et al.* should not be considered anticipatory prior art under 35 U.S.C. § 102(e).

### **III. The Examiner's Objections**

The Examiner has objected to claims 39-48, 56-76, and 80 as being dependent upon a rejected base claim, but that they would be allowable if rewritten in independent form, including all of the limitations of the base claim and any intervening claims.

Applicants respectfully submit that the submission herewith of a terminal disclaimer to obviate a double patenting rejection over prior U.S. Patent No. 6,821,726 renders the rejection of

claims 36-38 and 51-55 moot. Therefore, the objections to claims 39-48 and 56-63, which depend from claim 36, should also be rendered moot. Applicants note that the Examiner has also objected to claims 64-76 and 80. However, Applicants note that claim 64 is an independent claim, the Examiner has not maintained any rejections of claim 64 in the instant Office Action, and claims 65-76 depend from non-rejected claim 64. Therefore, Applicants submit that the Examiner's objections to claims 64-76 should be rendered moot because the Examiner has not maintained any rejections of claim 64. Finally, Applicants submit that claim 80 should be allowable because it depends from claim 77, which Applicants have argued above under paragraph II(B), should be allowable.

#### IV. Conclusion

In view of the above amendments and remarks, it is respectfully submitted that claims 36-48 and 51-87 are in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

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Customer No. 26633  
HELLER EHRMAN WHITE &  
MCAULIFFE LLP  
1717 Rhode Island Avenue, NW  
Washington, DC 20036-3001  
Telephone: (202) 912-2142  
Facsimile: (202) 912-2020

By Patricia D. Granados

Patricia D. Granados  
Attorney for Applicant  
Registration No. 33,683